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Set Items Description

S1 4458 PNEUMOLYS? OR PNEUMOCOC?

S2 98 S1 AND MODIF?

S3 18 S2 AND (MUTAT? OR MUTAGEN? OR MUTANT? ? OR POLYMORPH? OR P-  
OLY(W) (MORPHISM? ? OR MORPHIC?))

S4 14 RD (unique items)

? t 4/3,ab/1-14

- key terms

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4/3,AB/1 (Item 1 from file: 35)

DIALOG(R)File 35:Dissertation Abstracts Online

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01433152 AADAAI9533213

IMMUNE RESPONSES OF PNEUMOCOCCAL POLYSACCHARIDE AND CONJUGATE

VACCINES IN ADULTS: EFFECT OF HUMAN IMMUNODEFICIENCY VIRUS INFECTION  
(IMMUNE DEFICIENCY)

Author: AHMED, FARUQUE

Degree: PH.D.

Year: 1995

Corporate Source/Institution: THE JOHNS HOPKINS UNIVERSITY (0098)

Source: VOLUME 56/05-B OF DISSERTATION ABSTRACTS INTERNATIONAL.

PAGE 2584. 165 PAGES

Pneumococcal infection is an important cause of serious morbidity and mortality in the United States. The protective efficacy of the currently licensed pneumococcal polysaccharide vaccine is estimated to be about 60% in healthy adults, and is lower among high risk groups such as the elderly and the immunocompromised. Therefore, there is a need for a more immunogenic pneumococcal vaccine.

Searcher : Shears 308-4994

We evaluated whether the immunogenicity of an investigational protein-conjugate pneumococcal vaccine differs from that of the polysaccharide vaccine, whether the immune response is modified by HIV infection, and whether a secondary response can be elicited by a subsequent dose. This was assessed by randomizing 282 adults in Baltimore and Houston to receive either a protein-conjugate vaccine (containing capsular polysaccharides of pneumococcal serotypes 6B, 14, 18C, 19F, and 23F linked to a nontoxic mutant of diphtheria toxin) or the currently licensed polysaccharide vaccine. Randomization was stratified by HIV status, i.e., HIV seronegative, HIV seropositive with CD4 lymphocyte  $\geq 200/\mu\text{L}$ , and HIV seropositive with CD4 lymphocyte  $< 200/\mu\text{L}$ , within each enrollment site. Participants received the alternate vaccine at the 6-month visit. Blood samples were collected at enrollment and at the 1-, 6-, and 7-month visits.

The conjugate vaccine was observed to be more immunogenic than the polysaccharide vaccine in HIV-seronegative individuals, but not in HIV-infected persons. Among HIV-seronegative individuals, the adjusted immunoglobulin G antibody responses of the conjugate vaccine compared to the polysaccharide vaccine were 1.58 (95% confidence interval (CI) = 1.11, 2.24;  $P < 0.05$ ), 1.17 (95% CI = 0.73, 1.90), 3.41 (95% CI = 2.32, 5.01;  $P < 0.001$ ), 0.93 (95% CI = 0.71, 1.23), and 2.54 (95% CI = 1.73, 3.73;  $P < 0.001$ ) for serotypes 6B, 14, 18C, 19F, and 23F, respectively. The immunogenicities of both vaccines declined with increasingly severe immunodeficiency. Secondary responses were not observed in individuals primed with the conjugate vaccine, and vice-versa.

These data indicate that the conjugate vaccine is likely to be more effective than the polysaccharide vaccine in healthy adults; suggest that this effectiveness may be modified by HIV infection; and highlight the need to vaccinate HIV-infected persons early in the course of their infection.

4/3,AB/2 (Item 2 from file: 35)  
DIALOG(R)File 35:Dissertation Abstracts Online  
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1070331 AADD-86039

STUDIES OF PNEUMOLYSIN, THE MEMBRANE DAMAGING TOXIN OF STREPTOCOCCUS PNEUMONIAE

Author: WALKER, JOHN ARTHUR

Degree: PH.D.

Year: 1988

Corporate Source/Institution: UNIVERSITY OF LEICESTER (UNITED KINGDOM) (0451)

Source: VOLUME 50/05-B OF DISSERTATION ABSTRACTS INTERNATIONAL.  
PAGE 1778. 233 PAGES

Available from UMI in association with The British Library. Requires signed TDF.

Searcher : Shears 308-4994

A recombinant phage that produced a polypeptide possessing the characteristics of **pneumolysin**, the membrane damaging toxin of the **pneumococcus**, was isolated from a bank of **pneumococcal** sequences in  $\lambda$ gt10. Subclones carrying the **pneumolysin** gene in various plasmids were haemolytic regardless of the orientation of the insert.

The nucleotide sequence of a 5 kb fragment carrying the **pneumolysin** gene was determined. An open reading frame 1413 bp long was identified that when translated encoded a polypeptide with 471 amino acids and a molecular weight 52.8 kD. The N-terminal amino acid sequence of the predicted protein was identical to that of native **pneumolysin**. A single cysteine residue was present at position 428 in the amino acid sequence. Comparison of the DNA and amino acid sequences of **pneumolysin** with streptolysin O (SLO) revealed extensive homology in the amino acid sequence. The longest region of identity was a sequence of 12 amino acids surrounding the unique cysteine.

A hybrid gene consisting of the 5' region of the **pneumolysin** gene and the 3' end of the SLO gene was constructed. The fusion polypeptide was made in *E. coli*, but possessed a very low haemolytic activity.

Using the technique of oligonucleotide-mediated site-directed mutagenesis, two mutant genes were constructed in which the cysteine codon was changed to either a glycine or serine codon. Modified toxins when purified from *E. coli* had a specific activity of about 1-2% that of wild type **pneumolysin**.

4/3,AB/3 (Item 3 from file: 35)  
DIALOG(R)File 35:Dissertation Abstracts Online  
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785362 AAD8216013  
THE GENETICS OF MULTIPLE DRUG RESISTANCE IN STREPTOCOCCUS PNEUMONIAE  
Author: SMITH, MICHAEL DAVID  
Degree: PH.D.  
Year: 1982  
Corporate Source/Institution: DUKE UNIVERSITY (0066)  
Source: VOLUME 43/03-B OF DISSERTATION ABSTRACTS INTERNATIONAL.  
PAGE 628. 226 PAGES

The recent emergence of drug resistance in clinical isolates of *Streptococcus pneumoniae* (**pneumococcus**) suggested that plasmids had appeared in the species, but transformation experiments showed that the **pneumococcal** resistance genes were chromosomal. Some were mutations of the normal genome like those studied in laboratory **pneumococcus** years ago and some were on long inserts of DNA. Several clinical isolates were examined (B381, BM6001, BM4200 and others), and they appeared to contain similar but not identical insertions. The insertions carried genes often found on plasmids, including cat (chloramphenicol

Searcher : Shears 308-4994

acetyl transferase), aphA (aminoglycoside phosphotransferase), erm (ribosomal RNA **modification**), and tet (tetracycline resistance). Although no plasmids have appeared in the recent clinical isolates, **pneumococcus** accepted and maintained resistance plasmids isolated from other streptococci, and transferred them by transformation or by conjugation.

A novel property of the insertions was that some could transfer among streptococci and **pneumococci** by conjugation in the absence of plasmids. Insertions could retransfer from transconjugants in most cases. Plasmids (pIP501 and pMV158) introduced into strains that contained conjugative insertions co-existed with them without much interaction, although one insertion transposed to plasmid pAD1 in a *Streptococcus faecalis* background. A similar chromosomal insertion in *Streptococcus faecalis* is a transposon (Tn916) and a model proposed by Clewell and coworkers suggests that transposition is a part of the transfer process.

All conjugative insertions studied contained a tet gene, and almost all of the tet genes in them were homologous to each other but not to plasmid tet genes. Transformation experiments also showed extensive homology among various insertions in regions outside tet itself. The results suggested that a basic tet insertion, which is large enough to encode many other functions besides tet, acquired other resistance genes to create insertions carrying cat tet, tet erm, cat tet erm, or cat tet erm aphA in various strains.

In summary, clinical drug resistance in **pneumococcus** was found to be a combination of ordinary **mutation** and a novel tet-containing insertion that transferred between **pneumococcus** and related species. The spread of plasmid-type resistance mechanisms was apparently due to accumulation of genes near tet and subsequent transfer of the entire block by conjugation.

4/3,AB/4 (Item 1 from file: 144)  
DIALOG(R) File 144:Pascal  
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14050023 PASCAL No.: 99-0240270  
Penicillin-binding protein-mediated resistance in **pneumococci** and staphylococci

CHAMBERS H F  
Medical Service, San Francisco General Hospital, and Department of Medicine, University of California, San Francisco, United States  
Journal: The Journal of infectious diseases, 1999, 179 (SUP2) S353-S359  
Language: English

Target alteration underlies resistance to beta -lactam antibiotics in both *Staphylococcus* species and *Streptococcus pneumoniae*. The penicillin-binding protein (PBP) targets in penicillin-resistant strains of *S. pneumoniae* are **modified**, low-binding-affinity versions of the native PBPs. Multiple PBP targets may be **modified** by transformation

Searcher : Shears 308-4994

and homologous recombination with DNA from PBP genes of viridans streptococci. The level of resistance is determined by how many and to what extent targets are modified. In contrast, methicillin resistance in staphylococci is due to expression of PBP 2a, a novel, low-affinity PBP for which there is no homologue in methicillin-susceptible strains. PBP 2a is encoded by *mecA*, a highly conserved gene most likely acquired by a rare transposition from *Staphylococcus sciuri* or a closely related ancestor. Expression of resistance can be highly variable, but this seems not to be determined by PBP modifications. Several non-PBP factors are required for high-level resistance.

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4/3,AB/5 (Item 2 from file: 144)  
 DIALOG(R)File 144:Pascal  
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13590456 PASCAL No.: 98-0294489

Application of molecular typing to the epidemiology of *Streptococcus pneumoniae*

HALL L M C

Department of Medical Microbiology, St Bartholomew's and the Royal London School of Medicine and Dentistry, Turner Street, London E1 2AD, United Kingdom

Journal: Journal of clinical pathology, 1998, 51 (4) 270-274

Language: English

The spread of antibiotic resistance and the development of new vaccines have focused attention on the epidemiology of *Streptococcus pneumoniae* over recent years. While serotyping and the determination of antibiotic resistance remain primary methods for characterising pneumococci, molecular typing can add greater discrimination and complementary information. Methods based on restriction fragment length polymorphism within total DNA or non-specific polymerase chain reaction provide information representative of the whole genome and can be used to recognise closely related isolates from different sources, whether in the investigation of possible cross infection at the local level or in the investigation of national or international spread of antibiotic resistant strains. Fingerprinting of penicillin binding protein genes adds further information in the analysis of penicillin resistant isolates. The use of a combination of typing methods to analyse both the genome as a whole and specific loci has led to the realisation that pneumococci undergo horizontal gene transfer much more often than most other bacterial species. In particular the spread of penicillin resistance has been characterised by a combination of the spread of epidemic strains, transfer of chromosomal resistance genes from such strains into other genetic backgrounds, and transfer of capsule genes resulting in the switch of serotypes within strains. In the future molecular typing will have an important role in discovering whether widespread vaccination leads to

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genetic modification of the pneumococcal population causing invasive disease.

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4/3,AB/6 (Item 3 from file: 144)  
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12536191 PASCAL No.: 96-0213131

In vitro activities of U-100592 and U-100766, novel oxazolidinone antibacterial agents

ZURENKO G E; YAGI B H; SCHAADT R D; ALLISON J W; KILBURN J O; GLICKMAN S E; HUTCHINSON D K; BARBACHYN M R; BRICKNER S J

Cancer and Infectious Diseases Research, Pharmacia & Upjohn, Inc., 7000 Portage Rd., Kalamazoo, MI 49001-0199, United States

Journal: Antimicrobial agents and chemotherapy, 1996, 40 (4) 839-845

Language: English

Oxazolidinones make up a relatively new class of antimicrobial agents which possess a unique mechanism of bacterial protein synthesis inhibition. U-100592 ((S)-N-((3-(3-fluoro-4-(4-(hydroxyacetyl)-1-piperazinyl)-phenyl)-2-oxo-5-oxazolidinyl)methyl)-acetamide) and U-100766 ((S)-N-((3-(3-fluoro-4-(4-morpholinyl)phenyl)-2-oxo-5-oxazolidinyl)methyl)-acetamide) are novel oxazolidinone analogs from a directed chemical modification program. MICs were determined for a variety of bacterial clinical isolates; the respective MICs of U-100592 and U-100766 at which 90% of isolates are inhibited were as follows: methicillin-susceptible *Staphylococcus aureus*, 4 and 4 µg/ml; methicillin-resistant *S. aureus*, 4 and 4 µg/ml; methicillin-susceptible *Staphylococcus epidermidis*, 2 and 2 µg/ml; methicillin-resistant *S. epidermidis*, 1 and 2 µg/ml; *Enterococcus faecalis*, 2 and 4 µg/ml; *Enterococcus faecium*, 2 and 4 µg/ml; *Streptococcus pyogenes*, 1 and 2 µg/ml; *Streptococcus pneumoniae*, 0.50 and 1 µg/ml; *Corynebacterium* spp., 0.50 and 0.50 µg/ml; *Moraxella catarrhalis*, 4 and 4 µg/ml; *Listeria monocytogenes*, 8 and 2 µg/ml; and *Bacteroides fragilis*, 16 and 4 µg/ml. Most strains of *Mycobacterium tuberculosis* and the gram-positive anaerobes were inhibited in the range of 0.50 to 2 µg/ml. Enterococcal strains resistant to vancomycin (VanA, VanB, and VanC resistance phenotypes), pneumococcal strains resistant to penicillin, and *M. tuberculosis* strains resistant to common antitubercular agents (isoniazid, streptomycin, rifampin, ethionamide, and ethambutol) were not cross-resistant to the oxazolidinones. The presence of 10, 20, and 40% pooled human serum did not affect the antibacterial activities of the oxazolidinones. Time-kill studies demonstrated a bacteriostatic effect of the analogs against staphylococci and enterococci but a bactericidal effect against streptococci. The spontaneous mutation frequencies of *S. aureus* ATCC 29213 were  $<3.8 \times 10^{-8}$ .

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4/3,AB/7 (Item 4 from file: 144)  
DIALOG(R) File 144:Pascal  
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12407003 PASCAL No.: 96-0056686  
Epidemiologie moleculaire des pneumocoques resistants a la penicilline  
dans un hopital d'enfants a Paris  
(Molecular epidemiology of penicillin resistant *pneumococci* in a  
children's hospital in Paris)  
MOISSENET D; VU THIEN H  
Hop. enfants Armand Trousseau, serv. microbiologie, 75012 Paris, France  
Journal: L'Eurobiologiste : (Paris), 1995, 29 (220) 13-18  
Language: French Summary Language: English  
En France, depuis 1989, le nombre de pneumocoques resistants a la  
penicilline (PRP) ne cesse d'augmenter. La diminution de la sensibilite a  
la penicilline (et a l'ensemble des b-lactamines a des degres variables)  
est due a une **modification** des proteines de liaison a la penicilline  
(PLP), alterant leur affinite pour la penicilline. Trois PLP ont ete  
particulierement etudiees, 2b, 2x et 1a, et la sequence de leurs genes a  
ete determinee. Les PRP sont, par ailleurs, souvent multiresistants a de  
nombreuses familles d'antibiotiques. En 1993, 59 % des pneumocoques isoles  
a l'hopital d'enfants Armand Trousseau sont des PRP (CMI > 0,1 mg/l), et 87  
% d'entre eux avec un niveau de resistance eleve (CMI > 1 mg/l). Parmi les  
PRP, les isolats de serotype 9V arrivent en seconde position en terme de  
frequence, apres ceux du serotype 23F. Les PRP 9V presentent, en outre, une  
resistance constante au cotrimoxazole. Quatorze PRP 9V, provenant de pus  
d'otites, d'une arthrite et d'une hemoculture ont ete compares : profils de  
restriction chromosomique par electrophorese en champ pulse apres digestion  
de l'ADN par ApaI et profils de restriction des genes codant les PLP 2b, 2x  
et 1a apres amplification de l'ADN et digestion par Hinf I. Tous les PRP 9V  
presentent le meme pulsotype et le meme profil pour les genes 2b, 2x et 1a,  
evoquant une origine clonale. Tous les profils sont differents de ceux de  
la souche de reference R6, sensible a la penicilline, testee en parallele.  
La diffusion clonale represente, avec les transferts horizontaux de genes  
de PLP alteres et les **mutations** ponctuelles, les principaux  
mecanismes de la resistance aux beta -lactamines. Les marqueurs  
moleculaires, en apportant plus de precision que les methodes  
phenotypiques, permettent de mieux apprehender l'epidemiologie complexe de  
la resistance aux b-lactamines des pneumocoques et d'envisager des mesures  
pour resoudre cet important probleme de sante publique.

4/3,AB/8 (Item 5 from file: 144)  
DIALOG(R) File 144:Pascal  
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08842705 PASCAL No.: 90-0010568  
**Pneumolysin**, the thiol-activated toxin of *Streptococcus pneumoniae*,  
does not require a thiol group for in vitro activity

Searcher : Shears 308-4994

09/120044

SAUNDERS F K; MITCHELL T J; WALKER J A; ANDREW P W; BOULNOIS G J  
Univ. Leicester, dep. microbiology, Leicester LE1 9HN, United Kingdom  
Journal: Infection and immunity, 1989, 57 (8) 2547-2552  
Language: English

The role of the single cysteine residue in the activity of the thiol-activated toxin **pneumolysin** was investigated using oligonucleotide-mediated, site-directed **mutagenesis**. Three **modified** toxins in which the cysteine residue was changed to an alanine, a serine, or a glycine residue were purified to homogeneity and examined for activity. This suggests that the cysteine residue at position 428 is involved in neither the binding of toxin to membranes nor its insertion into the membrane, and also that the formation of oligomers is not by itself sufficient for toxin activity

4/3,AB/9 (Item 6 from file: 144)  
DIALOG(R)File 144:Pascal  
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04994194 PASCAL No.: 83-0246346  
**Mutagenesis** in *Streptococcus pneumoniae* (**pneumococcus**) by transformation with DNA **modified** by the carcinogen-mutagen, aflatoxin B SUB 1  
(**Mutagenese** chez *Streptococcus pneumoniae* (**pneumocoque**) par transformation avec du DNA **modifie** par le carcinogene **mutagene**, l'aflatoxine B SUB 1 )  
STARK A A; GIROUX C N  
Tel-Aviv univ., dep. biochemistry, Tel-Aviv 69978, Israel  
Journal: Mutation Research, 1983, 107 (1) 23-32  
Language: English Summary Language: English

4/3,AB/10 (Item 7 from file: 144)  
DIALOG(R)File 144:Pascal  
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04164589 PASCAL No.: 75-0000702  
MARKER DISCRIMINATION AND **MUTAGEN**-INDUCED ALTERATIONS IN **PNEUMOCOCCAL** TRANSFORMATION

TIRABY J-G; FOX M S  
DEP. BIOL., M.I.T., CAMBRIDGE, MASS. 02139  
Journal: GENETICS, 1974, 77 (3) 449-458  
Language: ENGLISH  
LA FONCTION RESPONSABLE DE LA DISCRIMINATION ENTRE LES MARQUEURS A HAUTE OU FAIBLE EFFICACITE DANS LA TRANSFORMATION DU PNEUMOCOQUE, ET RESPONSABLE DE L'ELIMINATION D'UNE FRACTION DES **MUTATIONS** SPONTANEEES, N'AGIT PAS SUR L'ADN INTEGRE TRANSPORTANT CES ALTERATIONS CHIMIQUES. LES **MODIFICATIONS** CHIMIQUES RESULTENT EN **MUTATIONS** QUI SONT EVIDENTES CHEZ LES BACTERIES TRANSFORMEES AVEC L'ADN TRAITE. LES  
Searcher : Shears 308-4994

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MUTANTS RESISTANT A L'ACIDE FUSIDIQUE SONT DE LA CLASSE A FAIBLE EFFICACITE. ON A MONTRE PRECEDEMMENT QUE LES MUTATIONS SPONTANEEES AYANT LIEU A CET ENDROIT SONT DE CLASSE A HAUTE EFFICACITE. LA DISCRIMINATION ELIMINERAIT LES APPARIEMENTS A:C ET G:T, ET LA TRANSFORMATIONS AVEC L'ADN MUTE ENTRAINERAIT UNE NON-RECONNAISSANCE DE CES APPARIEMENTS PAR LE SYSTEME DE DISCRIMINATION

4/3,AB/11 (Item 8 from file: 144)  
DIALOG(R)File 144:Pascal  
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04099509 PASCAL No.: 75-0001299  
LYMPHOCYTE AND POLYMORPHONUCLEAR ENZYMES IN STRESS. IV. CHANGES ASSOCIATED WITH AN ACUTE BACTERIAL INFECTION WITH DIPLOCOCCUS PNEUMONIAE (LES ENZYMES DES LYMPHOCYTES ET DES LEUCOCYTES DANS LE STRESS. IV. MODIFICATIONS ASSOCIEES A UNE INFECTION BACTERIENNE AIGUE A D. P.)

LEISE E M; LESANE F; GRAY I  
DEP. BIOL., GEORGETOWN UNIV., WASHINGTON, D.C. 20007  
Journal: BIOCHEM. MED., 1974, 9 (3) 206-213  
Language: ENGLISH

LES LEUCOCYTES EN PARTICULIER LES LYMPHOCYTES DU SOMMET D'UN GRADIENT DE DEXTRANE DE DENSITE 1,060, PEUVENT SERVIR D'INDICATEURS PRECOCES SENSIBLES DE L'EXPOSITION A UNE INFECTION BACTERIENNE. LES C DE PROTEINES DANS CES CELLULES DE LAPINS INFECTES PAR D. PNEUMONIAE AUGMENTENT RAPIDEMENT ET RESTENT ELEVEE PENDANT TOUTE L'INFECTION. UNE AUGMENTATION DE LA C DE PROTEINES DES LYMPHOCYTES DU TYPE C1 DE PLUS DE 25% AU-DESSUS D'UNE MOYENNE PRECEDEMMENT ETABLIE PEUT SUGGERER UNE EXPOSITION A UN AGENT BACTERIEN. LA C DE LDH DANS CES CELLULES N'AUGMENTE PAS TOUJOURS PROPORTIONNELLEMENT A L'AUGMENTATION DES PROTEINES. TOUTEFOIS EN CAS D'ELEVATION EXCESSIVE DE LA LDH C1, CELLE-CI PEUT CORROBORER L'APPRECIATION D'UNE EXPOSITION A UN AGENT BACTERIEN

4/3,AB/12 (Item 9 from file: 144)  
DIALOG(R)File 144:Pascal  
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00918571 PASCAL No.: 76-0020232  
A MODIFIER MUTATION AFFECTING UTILIZATION OF MANNITOL IN PNEUMOCOCCUS

ROTHEIM M B; HOTCHKISS R D  
STATE UNIV. NEW YORK, UPSTATE MED. CENT., SYRACUSE, N.Y. 13210  
Journal: CANAD. J. MICROBIOL., 1975, 21 (8) 1139-1143  
Language: ENGLISH Summary Language: FRENCH  
ON DECRIT LA CROISSANCE MODIFIEE D'UN MUTANT DE PNEUMOCOQUE PORTANT UN MARQUEUR M RESPONSABLE DE L'UTILISATION DU MANNITOL ET UN GENE MODIFICATEUR. CE DERNIER EST ETROITEMENT LIE AU GENE M ET FAIT QUE LA CULTURE SUR MILIEU AU MANNITOL N'EST POSSIBLE QU'APRES PRE-CULTURE DANS DU  
Searcher : Shears 308-4994

09/120044

GLUCOSE A 0,4%. LA POSITION DU GENE M SERAIT ERY-R STR-R M SUL-RD

4/3,AB/13 (Item 10 from file: 144)  
DIALOG(R)File 144:Pascal  
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00606974 PASCAL No.: 74-0005822  
INTEGRATION EFFICIENCY IN DNA-INDUCED TRANSFORMATION OF  
PNEUMOCOCCUS. I. A METHOD OF TRANSFORMATION IN SOLID MEDIUM AND ITS  
USE FOR ISOLATION OF TRANSFORMATION-DEFICIENT AND RECOMBINATION-  
MODIFIED MUTANTS

(EFFICACITE DE L'INTEGRATION DANS LA TRANSFORMATION INDUITE PAR DNA CHEZ  
P. I. METHODE DE TRANSFORMATION EN MILIEU SOLIDE ET SON UTILISATION POUR  
L'ISOLEMENT DE MUTANTS DEFICIENTS POUR LA TRANSFORMATION ET A  
RECOMBINAISON MODIFIEE)

TIRABY G; CLAVERYS J-P; SICARD M A  
LAB. GENET., UNIV. PAUL SABATIER, TOULOUSE, FRANCE  
Journal: GENETICS, 1973, 75 (1) 23-33  
Language: ENGLISH

SOUS CONDITIONS SPECIFIQUES TOUTES LES COLONIES CULTIVEES EN PRESENCE DE  
DNA TRANSFORMANT PENDANT 6HEURES DONNENT LIEU A DES BACTERIES TRANSFORMEES.  
CETTE TECHNIQUE PERMET D'ISOLER DES MUTANTS DE RECOMBINAISON. LA  
PLUPART D'ENTRE EUX SONT DEFECTIFS POUR LA TRANSFORMATION ET PRESENTENT UNE  
GRANDE DIVERSITE DANS LEUR REPONSE AUX U.V. ON ISOLE AUSSI DES  
MUTANTS QUI ONT UN COMPORTEMENT ALTERE QUANT A L'EFFICACITE DES  
MARQUEURS

4/3,AB/14 (Item 1 from file: 266)  
DIALOG(R)File 266:FEDRIP  
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00306143  
IDENTIFYING NO.: Z01DE00690-01 AGENCY CODE: CRISP  
PATHOGENIC MECHANISMS OF MICROORGANISMS--VACCINE AND PEUTIC APPLICATION  
PRINCIPAL INVESTIGATOR: KEITH, J M  
ADDRESS: NIDCR, NIH  
SPONSORING ORG.: NATIONAL INSTITUTE OF DENTAL & CRANIOFACIAL RESEARCH  
FY : 1999

SUMMARY: search efforts focus on vaccine and therapeutic development  
through both basic and applied research projects. Studies are designed to  
increase our understanding of pathogenic mechanisms associated with  
microbial infections and devise novel vaccine and therapeutics strategies  
to protect humans from the sever effects of infectious diseases. In recent  
research studies, our laboratory determined the molecular mechanism  
responsible for antibiotic resistance in several clinical isolates of  
Streptococcus pneumoniae from patients at Children's Hospital in  
Washington, DC . In one study, we demonstrated that a specific single amino  
Searcher : Shears 308-4994

09/120044

acid **mutation** in the bacterial chromosomal gene for dihydrofolate reductase was responsible for high level trimethoprim resistance seen in these **pneumococcal** clinical isolates. In a similar study, we have isolated and characterized the molecular determinant responsible for optochin resistance in *S. pneumoniae*. This is the first reported cases of infection with *S. pneumoniae* in the United States that can not be detected by the optochin resistance/sensitive diagnosis test. We have isolated the gene and the **mutation** responsible for failure of this strain to be detected by the clinical laboratory test. In addition to this research, the laboratory continues to work on the development of genetically detoxified pertussis toxin for acellular whooping cough vaccines. Whooping cough is an upper respiratory tract infection caused by *Bordetella pertussis*. resulting in mortality rates estimated at about 500,000 deaths per year. This disease has been effectively controlled by the current vaccine which consists of killed whole *B. pertussis* cells. Although efficacious, the present whole cell vaccine produces unacceptable side effects. The major protective antigen in whooping cough vaccines is pertussis toxin. Chemically inactivated pertussis toxin vaccines have been produced with reduced side effects and reasonable efficacy, however, these product suffer from reduced antigenicity and difficulties in vaccine manufacture processing. In addition, residual activity may exist from reversion or incomplete chemical inactivation. Using site-specific DNA **mutagenesis**, we **modified** *E. coli* subclones of pertussis toxin and used these constructs to replace the chromosomal copy of the toxin gene in *B. pertussis* vaccine strain 3779. The resulting new strain produces a fully genetically detoxified form of pertussis toxin which is strongly immunoprotective and can be used as a vaccine antigen without chemical inactivation. In a recently competed NIAID-supported clinical trial in Sweden and Italy, pertussis toxin emerged as an essential component of any new whooping cough vaccine. One of the most successful acellular pertussis vaccines used in this clinical trail contained a genetically altered version of pertussis toxin that was developed from basic research generated through this intramural research project. Molecular studies are currently underway in our laboratory to develop higher yield bacterial strains to enhance expression of pertussis toxin for use in acellular and conjugate vaccine manufacture. In addition, an avirulent, live attenuated *B. pertussis* vaccine is being developed which is capable of delivering other immunoprotective antigens such as proteins from HIV, TB, and hepatitis C virus and well as the protective pertussis antigens."

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Set	Items	Description
S5	0	PNVJ1 OR PNVJ20 OR PNVJ22 OR PNVJ45 OR PNVJ56 OR PNV103 OR PNV207 OR PNV111 OR PNV211 OR PNVJ(W) (1 OR 20 OR 22 OR 45 OR - 56) OR PNV(W) (103 OR 207 OR 111 OR 211)

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Searcher : Shears 308-4994

Named poly-peptides  
claims 7-15

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*           U. S.   P A T E N T   T E X T   F I L E           *
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* THROUGH AUGUST 31,1999                                         *
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terms  
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L1 832 SEA FILE=USPAT PNEUMOCOC? OR PNEUMOLYS?  
L5 4 SEA FILE=USPAT L1(5A)MODIF?

L1 832 SEA FILE=USPAT PNEUMOCOC? OR PNEUMOLYS?  
L2 593 SEA FILE=USPAT L1 AND MODIF?  
L3 235 SEA FILE=USPAT L2 AND (MUTAT? OR MUTAGEN? OR MUTANT# OR PO-  
LYMORPHISM# OR POLYMORPHIC? OR POLY(W) (MORPHIC? OR MORPHISM#))  
L4 58 SEA FILE=USPAT L3 AND ATTENUAT?  
L9 8 SEA FILE=USPAT L4 AND (HEMOLYT? OR HAEMOLYT?)

=> s 15 or 19

L10 12 L5 OR L9

=> d 1-12 .bevpat

US PAT NO: 5,872,104 [IMAGE AVAILABLE] L10: 1 of 12  
TITLE: Combinations and methods for reducing antimicrobial  
resistance  
DATE ISSUED: Feb. 16, 1999  
INVENTOR: Nicolaas M. J. Vermeulen, Woodinville, WA  
Dennis E. Schwartz, Redmond, WA  
SEARCH-FLD: 514/29, 303, 30, 35, 46; 536/7.2

# ABSTRACT:

Disclosed are novel methods, combinations of agents and kits for use in killing, or inhibiting the growth of, microorganisms. Enhanced antimicrobial action is provided by using a methylation inhibitor, as exemplified by using an agent that inhibits methylation or maturation of bacterial RNA in combination with, e.g., a macrolide lincosamide streptogramin B (MLS) antibiotic. The methods and compositions described may be employed to reduce the resistance of susceptible microorganisms to antimicrobial agents and thus to treat animals or patients with infections.

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US PAT NO: 5,854,416 [IMAGE AVAILABLE] L10: 2 of 12  
TITLE: Streptococcus pneumoniae 37-KDA surface adhesin a protein  
and nucleic acids coding therefor  
DATE ISSUED: Dec. 29, 1998  
INVENTOR: Jacquelyn S. Sampson, College Park, GA  
Harold Russell, Atlanta, GA  
Jean A. Tharpe, Lithonia, GA  
Edwin W. Ades, Atlanta, GA  
George M. Carlone, Stone Mountain, GA  
SEARCH-FLD: 536/23.7, 23.1; 435/320.1; 424/244.1

ABSTRACT:

The invention provides a nucleic acid encoding the 37-kDa protein from Streptococcus pneumoniae. Also provided are isolated nucleic acids comprising a unique fragment of at least 10 nucleotides of the 37-kDa protein. The invention also provides purified polypeptides encoded by the nucleic acid encoding the 37-kDa protein from and the nucleic acids comprising a unique fragment of at least 10 nucleotides of the 37-kDa protein. Also provided are antibodies which selectively binds the polypeptides encoded by the nucleic acid encoding the 37-kDa protein and the nucleic acids comprising a unique fragment of at least 10 nucleotides of the 37-kDa protein. Also provided are vaccines comprising immunogenic polypeptides encoded by the nucleic acid encoding the 37-kDa protein and the nucleic acids comprising a unique fragment of at least 10 nucleotides of the 37-kDa protein. Further provided is a method of detecting the presence of Streptococcus pneumoniae in a sample comprising the steps of contacting a sample suspected of containing Streptococcus pneumoniae with nucleic acid primers capable of hybridizing to a nucleic acid comprising a portion of the nucleic acid encoding the 37-kDa protein, amplifying the nucleic acid and detecting the presence of an amplification product, the presence of the amplification product indicating the presence of Streptococcus pneumoniae in the sample. Further provided are methods of detecting the presence of Streptococcus pneumoniae in a sample using antibodies or antigens, methods of preventing and treating Streptococcus pneumoniae infection in a subject.

US PAT NO: 5,837,533 [IMAGE AVAILABLE] L10: 3 of 12  
TITLE: Complexes comprising a nucleic acid bound to a cationic  
polyamine having an endosome disruption agent  
DATE ISSUED: Nov. 17, 1998  
INVENTOR: Raymond H. Boutin, Thornton, PA  
SEARCH-FLD: 435/320.1, 172.3; 424/93.21; 514/44; 935/54, 52

ABSTRACT:

A multifunctional molecular complex for the transfer of a nucleic acid composition to a target cell is provided which comprises in any functional combination: A) said nucleic acid composition; and B) a transfer moiety comprising 1) one or more cationic polyamine components bound to said nucleic acid composition, each comprising from three to twelve nitrogen atoms; 2) one or more endosome membrane disruption

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promoting components attached to at least one nitrogen atom of at least one of said polyamine components, through an alkyl, carboxamide, carbamate, thiocarbamate, or carbamoyl bridging group, comprising a) at least one lipophilic long chain alkyl group, b) a fusogenic peptide comprising spike glycoproteins of enveloped animal viruses, or c) cholic acid or cholesteryl or derivatives; and optionally 3) one or more receptor specific binding components which are ligands for natural receptors of said target cell, attached through an alkyl, carboxamide, carbamate, thiocarbamate, or carbamoyl bridging group to either i) a further nitrogen atom of at least one of said polyamine components to which said one or more endosome membrane disruption promoting components is attached, or ii) a nitrogen atom of at least one further polyamine component which does not have attached thereto any endosome membrane disruption promoting component. Also provided are the transfer moiety alone, or in combination with the nucleic acid composition as a self-assembling combination, and the use of these compositions in methods for transferring nucleic acid compositions to cells or to cells of individuals, for immunizing individuals against a pathogen or disease, and for treating an individual with a disease.

US PAT NO: 5,830,876 [IMAGE AVAILABLE] L10: 4 of 12  
 TITLE: Genetic immunization  
 DATE ISSUED: Nov. 3, 1998  
 INVENTOR: David B. Weiner, Merion, PA  
 William V. Williams, Havertown, PA  
 Bin Wang, Havertown, PA  
 SEARCH-FLD: 435/320.1; 424/93.1, 93.2, 93.21, 278.1; 514/44, 615, 818

## ABSTRACT:

A method of immunizing an individual against pathogen is disclosed. Also disclosed is a method of treating an individual who has a hyperproliferative disease, or of treating an individual who is infected by a pathogen. Specifically, the individual is injected with bupivacaine along with DNA in an expressible form, the DNA encoding an antigen. The encoded antigen can be from a protein from the pathogen or from a protein associated with the hyperproliferative disease.

US PAT NO: 5,817,637 [IMAGE AVAILABLE] L10: 5 of 12  
 TITLE: Genetic immunization  
 DATE ISSUED: Oct. 6, 1998  
 INVENTOR: David B. Weiner, Merion, PA  
 William V. Williams, Havertown, PA  
 Bin Wang, Havertown, PA  
 SEARCH-FLD: 514/44, 615, 818; 424/278.1; 435/975

## ABSTRACT:

Methods of prophylactic and therapeutic immunization of an individual against pathogen infection, diseases associated with hyperproliferative cells and autoimmune diseases are disclosed. The methods comprise the steps of administering to cells of an individual, a nucleic acid molecule that comprises a nucleotide sequence that encodes a protein which

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comprises at least one epitope that is identical or substantially similar to an epitope of a pathogen antigen, a hyperproliferative cell associated protein or a protein associated with autoimmune disease respectively. In each case, nucleotide sequence is operably linked to regulatory sequences to enable expression in the cells. The nucleic acid molecule is free of viral particles and capable of being expressed in said cells. The cells may be contacted cells with a cell stimulating agent. Methods of prophylactically and therapeutically immunizing an individual against HIV are disclosed. Pharmaceutical compositions and kits for practicing methods of the present invention are disclosed.

US PAT NO: 5,739,118 [IMAGE AVAILABLE] L10: 6 of 12  
TITLE: Compositions and methods for delivery of genetic material  
DATE ISSUED: Apr. 14, 1998  
INVENTOR: Richard A. Carrano, Paoli, PA  
Bin Wang, Beijing, China  
David B. Weiner, Merion, PA  
SEARCH-FLD: 435/172.3, 69.1, 69.3, 375, 377; 514/44, 33, 35, 171, 27,  
54, 510, 680, 731, 732, 25, 26; 424/278.1, 184.1;  
935/52, 55, 56; 536/23.1, 23.5, 23.7, 23.72, 24.5

ABSTRACT:

Methods of introducing genetic material into cells of an individual and compositions and kits for practicing the same are disclosed. The methods comprise the steps of contacting cells of an individual with a genetic vaccine facilitator and administering to the cells, a nucleic acid molecule that is free of retroviral particles. The nucleic acid molecule comprises a nucleotide sequence that encodes a protein that comprises at least one epitope that is identical or substantially similar to an epitope of a pathogen antigen or an antigen associated with a hyperproliferative or autoimmune disease, a protein otherwise missing from the individual due to a missing, non-functional or partially functioning gene, or a protein that produce a therapeutic effect on an individual. Methods of prophylactically and therapeutically immunizing an individual against HIV are disclosed. Pharmaceutical compositions and kits for practicing methods of the present invention are disclosed.

US PAT NO: 5,679,768 [IMAGE AVAILABLE] L10: 7 of 12  
TITLE: Epitopic regions of pneumococcal surface protein A  
DATE ISSUED: Oct. 21, 1997  
INVENTOR: David E. Briles, Birmingham, AL  
Janet L. Yother, Birmingham, AL  
SEARCH-FLD: 424/244.1, 190.1, 197.11, 200.1; 530/300, 324, 350, 825;  
435/252.3

ABSTRACT:

A region of the PspA protein of the Rx1 strain of Streptococcus pneumoniae has been identified as containing protection-eliciting epitopes which are cross-reactive with PspAs of other S.pneumoniae strains. The region comprises the 68-amino acid sequence extending from amino acid residues 192 to 260 of the Rx1 PspA strain.

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US PAT NO: 5,593,972 [IMAGE AVAILABLE] L10: 8 of 12  
TITLE: Genetic immunization  
DATE ISSUED: Jan. 14, 1997  
INVENTOR: David B. Weiner, Merion, PA  
William V. Williams, Havertown, PA  
Bin Wang, Havertown, PA  
SEARCH-FLD: 435/320.1; 424/93.1, 93.2, 93.21, 278.1; 514/44, 615, 818

ABSTRACT:

Methods of prophylactic and therapeutic immunization of an individual against pathogen infection, diseases associated with hyperproliferative cells and autoimmune diseases are disclosed. The methods comprise the steps of administering to cells of an individual, a nucleic acid molecule that comprises a nucleotide sequence that encodes a protein which comprises at least one epitope that is identical or substantially similar to an epitope of a pathogen antigen, a hyperproliferative cell associated protein or a protein associated with autoimmune disease respectively. In each case, nucleotide sequence is operably linked to regulatory sequences to enable expression in the cells. The nucleic acid molecule is free of viral particles and capable of being expressed in said cells. The cells may be contacted cells with a cell stimulating agent. Methods of prophylactically and therapeutically immunizing an individual against HIV are disclosed. Pharmaceutical compositions and kits for practicing methods of the present invention are disclosed.

US PAT NO: 5,556,757 [IMAGE AVAILABLE] L10: 9 of 12  
TITLE: Peptides representing epitopic sites for bacterial and  
viral meningitis causing agents and their CNS carrier  
and uses thereof  
DATE ISSUED: Sep. 17, 1996  
INVENTOR: Diane V. Alstyne, Vancouver, Canada  
Lawrence R. Sharma, Vancouver, Canada  
SEARCH-FLD: 435/7.2, 7.32, 7.34; 530/300, 324, 327, 329; 514/2

ABSTRACT:

Peptides comprising a Meningitis Related Homologous Antigenic Sequence (MRHAS) are provided. The MRHAS is found in meningitis-causing organisms and chemokines involved in cell chemotaxis. The peptides are useful as antigens and vaccines for detection, diagnosis and treatment of meningitis.

US PAT NO: 5,510,264 [IMAGE AVAILABLE] L10: 10 of 12  
TITLE: Antibodies which bind meningitis related homologous  
antigenic sequences  
DATE ISSUED: Apr. 23, 1996  
INVENTOR: Diane Van Alstyne, Vancouver, Canada  
Lawrence R. Sharma, Vancouver, Canada  
SEARCH-FLD: 530/388.3, 388.4, 387.9, 388.2, 388.23; 435/240.27, 7.2;  
424/147.1, 150.1

ABSTRACT:

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Monoclonal antibodies capable of binding to a Meningitis Related Homologous Antigenic Sequence (MRHAS) are provided. The MRHAS is found in meningitis-causing organisms and chemokines involved in cell chemotaxis. The monoclonal antibodies are useful for detection and diagnosis of meningitis.

US PAT NO: 5,272,258 [IMAGE AVAILABLE] L10: 11 of 12  
TITLE: Monoclonal antibodies to C-reactive protein  
DATE ISSUED: Dec. 21, 1993  
INVENTOR: Joan N. Siegel, Oak Park, IL  
Lawrence A. Potempa, Deerfield, IL  
Henry Gewurz, Evanston, IL  
SEARCH-FLD: 435/7, 240.27, 7.1, 7.2; 530/380, 387, 388.25

ABSTRACT:

The invention comprises monoclonal antibodies reactive with native C-reactive protein (CRP) and modified CRP having the specificities described herein. The invention also comprises the hybridomas used to produce these antibodies. The antibodies may be used to detect or quantitate native CRP and modified CRP, and kits for performing such assays are part of the invention.

US PAT NO: 4,830,852 [IMAGE AVAILABLE] L10: 12 of 12  
TITLE: Covalently-modified neutral bacterial polysaccharides, stable covalent conjugates of such polysaccharides and immunogenic proteins and methods of preparing such polysaccharides and conjugates  
DATE ISSUED: May 16, 1989  
INVENTOR: Stephen Marburg, Metuchen, NJ  
Richard L. Tolman, Warren, NJ  
Deborah A. Jorn, Metuchen, NJ  
SEARCH-FLD: 424/88, 92; 530/395, 402-406; 536/55.1, 1.1, 123; 514/54

ABSTRACT:

Covalently-modified neutral bacterial polysaccharides; covalent conjugates of such polysaccharides linked by a bigeneric spacer, with immunogenic bacterial membrane or other proteins, which conjugates are useful components of bacterial vaccines; and methods of preparing such polysaccharides and conjugates.

=> d his l11-l14; d l14 1-37 .bevpat

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L11 480 S L1(L)MODIF?  
L12 177 SEA L11(L) (MUTAT? OR MUTAGEN? OR MUTANT# OR POLYMORPHISM#  
OR POLYMORPHIC? OR POLY(W) (MORPHIC? OR MORPHISM#))  
L13 42 S L12(L)ATTENUAT?  
L14 37 S L13 NOT L10

US PAT NO: 5,935,570 [IMAGE AVAILABLE] L14: 1 of 37  
Searcher : Shears 308-4994

09/120044

TITLE: Synthesis of immunologic, therapeutic and prophylactic compounds by transformed clavibacter

DATE ISSUED: Aug. 10, 1999

INVENTOR: Hilary Koprowski, Wynnewood, PA  
Peter Spikins Carlson, Alexandria, VA  
Douglas Craig Hooper, Medford, NJ  
Laura Jane Conway, Haverford, PA  
Frank H. Michaels, Havertown, PA  
Anna Modelska, Wynnewood, PA  
Zhen Fang Fu, Cherry Hill, NJ

SEARCH-FLD: 424/192.4, 93.461, 93.4, 184.1, 224.1, 93.2; 435/69.1, 69.3, 172.1, 71.1, 71.2, 410, 419, 252.3; 530/350; 536/23.7; 800/279, 288, 298

ABSTRACT:

A process for the synthesis and delivery of bioactive compounds, compounds that have a therapeutic, biochemical, or immunologic, effect on an animal, such as human. In the process, clavibacter is genetically altered so that it synthesizes the bioactive compound. A plant may be infected with the genetically altered clavibacter and used as an oral delivery system.

US PAT NO: 5,932,222 [IMAGE AVAILABLE] L14: 2 of 37

TITLE: Mutant respiratory syncytial virus (RSV), vaccines containing same and methods of use

DATE ISSUED: Aug. 3, 1999

INVENTOR: Valerie B. Randolph, Lincoln Park, NJ  
Joan C. Crowley, Englewood, NJ

SEARCH-FLD: 424/89, 211.1, 278.1, 88; 435/237

ABSTRACT:

This invention provides cold adapted mutant RSV, specifically, mutant RSV of subgroup A and B. Nucleic acid molecules encoding the mutant RSV of this invention, and immunogenic polypeptides of these mutant RSV also are provided by this invention. Pharmaceutical compositions containing any of the above compositions are provided herein. These are especially useful as vaccines. Further provided by this invention are methods of vaccinating a subject against RSV infection using the pharmaceutical compositions described herein.

US PAT NO: 5,928,900 [IMAGE AVAILABLE] L14: 3 of 37

TITLE: Bacterial exported proteins and acellular vaccines based thereon

DATE ISSUED: Jul. 27, 1999

INVENTOR: H. Robert Masure, New York, NY  
Barbara J. Pearce, New York, NY  
Elaine Tuomanen, New York, NY

SEARCH-FLD: 530/350; 424/185.1, 190.1, 244.1; 435/69.3

ABSTRACT:

The present invention relates to the identification of Gram positive

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bacterial exported proteins, and the genes encoding such proteins. In particular, the invention relates to adhesion associated exported proteins, and to antigens common to many or all strains of a species of Gram positive bacterium. The invention also relates to acellular vaccines to provide protection from Gram positive bacterial infection using such genes or such proteins, and to antibodies against such proteins for use in diagnosis and passive immune therapy. In specific embodiments, fragments of ten genes encoding exported proteins of *S. pneumoniae* are disclosed, and the functional activity of some of these proteins in adherence is demonstrated.

US PAT NO: 5,917,017 [IMAGE AVAILABLE] L14: 4 of 37  
 TITLE: Diphtheria toxin vaccines bearing a mutated R domain  
 DATE ISSUED: Jun. 29, 1999  
 INVENTOR: R. John Collier, Wellesley Hills, MA

Wei Hai Shen, Boston, MA  
 David Eisenberg, Los Angeles, CA  
 Seunghyon Choe, Solana Beach, CA

SEARCH-FLD: 424/203.1, 183.1, 184.1, 185.1, 236.1, 245.1, 239.1;  
 530/350; 435/69.1, 69.7, 29

#### ABSTRACT:

Diphtheria toxin polypeptides comprising a mutant R binding domain exhibit reduced target cell binding and may be used as vaccines to immunize a mammal against infection by *Corynebacterium diphtheria*.

US PAT NO: 5,908,629 [IMAGE AVAILABLE] L14: 5 of 37  
 TITLE: Conjugate vaccine for group B streptococcus  
 DATE ISSUED: Jun. 1, 1999  
 INVENTOR: James L. Michel, Waban, MA

Dennis L. Kasper, Newton Centre, MA  
 Frederick M. Ausubel, Newton, MA  
 Lawrence C. Madoff, Boston, MA

SEARCH-FLD: 424/197.11, 237.1, 244.1; 435/69.3, 172.1; 530/350, 403,  
 825; 536/23.7

#### ABSTRACT:

A vaccine capable of protecting a recipient from infection caused by group B Streptococcus. The vaccine provides polysaccharide-protein moieties and contain (a) a group B Streptococcus polysaccharide conjugated to (b) a functional derivative of a group B Streptococcus C protein alpha antigen that retains the ability to elicit protective antibodies against group B Streptococcus. The vaccine may contain only one type of such polysaccharide-protein unit or may contain a mixture of more than one type of unit.

US PAT NO: 5,891,438 [IMAGE AVAILABLE] L14: 6 of 37  
 TITLE: Method for stimulating production of variable region gene family restricted antibodies through B-cell superantigen vaccination

DATE ISSUED: Apr. 6, 1999

INVENTOR: Gregg J. Silverman, Encinitas, CA

Searcher : Shears 308-4994

09/120044

SEARCH-FLD: 424/130.1, 184.1, 201.1, 203.1, 185.1, 234.1; 514/2, 8,  
12, 23, 54; 530/300, 324

ABSTRACT:

Criteria for identifying potential B cell superantigens are disclosed, together with a method for determining whether these candidate antigens have B cell superantigenic activity. Methods for constructing and using a vaccine including B cell superantigens are also disclosed. Identification is based on characterizing the structure of Ig binding sites which interact with the candidate antigen assessment of Ig V region diversity on binding of candidate and conventional antigens, confirmation of sAg activity in interactions between candidate antigens and whole cells, confirmation of whether the candidate antigen induces B cell mitogenesis, determination of the earliest point in B cell development where cellular co-factors are required for sAg activity and, for reference, determination of V region usage in responder populations. Once a B cell superantigen is characterized, it is purified and conjugated by chemical means to a polysaccharide or glycoprotein component from a microbial capsule, cell wall, envelope or other component preferably using components which stimulate production of antibodies with the same V region restriction as antibodies whose production is stimulated by the B cell superantigen.

US PAT NO: 5,876,931 [IMAGE AVAILABLE] L14: 7 of 37  
TITLE: Identification of genes  
DATE ISSUED: Mar. 2, 1999  
INVENTOR: David William Holden, London, United Kingdom  
SEARCH-FLD: 435/172.1, 172.3, 252.1, 252.3, 243, 4, 6; 424/93.2, 93.4;  
530/350; 536/23.1, 23.7

ABSTRACT:

A method for identifying a microorganism having a reduced adaptation to a particular environment comprising the steps of:

- (1) providing a plurality of microorganisms each of which is independently mutated by the insertional inactivation of a gene with a nucleic acid comprising a unique marker sequence so that each mutant contains a different marker sequence, or clones of the said microorganism;
- (2) providing individually a stored sample of each mutant produced by step (1) and providing individually stored nucleic acid comprising the unique marker sequence from each individual mutant;
- (3) introducing a plurality of mutants produced by step (1) into the said particular environment and allowing those microorganisms which are able to do so to grow in the said environment;
- (4) retrieving microorganisms from the said environment or a selected part thereof and isolating the nucleic acid from the retrieved microorganisms;
- (5) comparing any marker sequences in the nucleic acid isolated in step

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(4) to the unique marker sequence of each individual mutant stored as in step (2); and

(6) selecting an individual mutant which does not contain any of the marker sequences as isolated in step (4).

US PAT NO: 5,858,362 [IMAGE AVAILABLE] L14: 8 of 37  
 TITLE: Conjugate vaccine for group B Streptococcus  
 DATE ISSUED: Jan. 12, 1999  
 INVENTOR: James L. Michel, Waban, MA  
 Dennis L. Kasper, Newton Centre, MA  
 Frederick M. Ausubel, Newton, MA  
 Lawrence C. Madoff, Boston, MA  
 SEARCH-FLD: 424/165.1, 197.11; 435/69.3, 172.1; 530/350, 403, 825;  
 536/23.7

#### ABSTRACT:

A vaccine capable of protecting a recipient from infection caused by group B Streptococcus. The vaccine provides polysaccharide-protein moieties and contain (a) a group B Streptococcus polysaccharide conjugated to (b) a functional derivative of a group B Streptococcus C protein alpha antigen that retains the ability to elicit protective antibodies against group B Streptococcus. The vaccine may contain only one type of such polysaccharide-protein unit or may contain a mixture of more than one type of unit.

US PAT NO: 5,856,170 [IMAGE AVAILABLE] L14: 9 of 37  
 TITLE: Structural gene of pneumococcal protein  
 DATE ISSUED: Jan. 5, 1999  
 INVENTOR: David E. Briles, Birmingham, AL  
 Janet L. Yother, Birmingham, AL  
 SEARCH-FLD: 435/253.7, 253.1, 69.3, 252.33; 535/23.7

#### ABSTRACT:

A purified pneumococcal surface protein A (PspA) comprises a truncated form of the PspA protein which is immunoprotective and contains the protective epitopes of PspA. The PspA protein is soluble in physiologic solution and lacks at least the cell membrane anchor region of the whole protein. The protein is formed by insertion-duplication of mutagenesis of *S. pneumoniae* with *pspA* gene and expression of the truncated protein into the growth medium.

US PAT NO: 5,847,081 [IMAGE AVAILABLE] L14: 10 of 37  
 TITLE: Conjugate vaccine for group B Streptococcus  
 DATE ISSUED: Dec. 8, 1998  
 INVENTOR: James L. Michel, Waban, MA  
 Dennis L. Kasper, Newton Centre, MA  
 Frederick M. Ausubel, Newton, MA  
 Lawrence C. Madoff, Boston, MA  
 SEARCH-FLD: 435/253.4, 69.3; 424/244.1; 536/23.7; 530/350

#### ABSTRACT:

A vaccine capable of protecting a recipient from infection caused by

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group B Streptococcus. The vaccine provides polysaccharide-protein moieties and contain (a) a group B Streptococcus polysaccharide conjugated to (b) a functional derivative of a group B Streptococcus C protein alpha antigen that retains the ability to elicit protective antibodies against group B Streptococcus. The vaccine may contain only one type of such polysaccharide-protein unit or may contain a mixture of more than one type of unit.

US PAT NO: 5,843,711 [IMAGE AVAILABLE] L14: 11 of 37  
 TITLE: Diphtheria toxin receptor-binding region  
 DATE ISSUED: Dec. 1, 1998  
 INVENTOR: R. John Collier, Wellesley Hills, MA  
 David Eisenberg, Los Angeles, CA  
 Haian Fu, Allston, MA  
 Seunghyon Choe, Reseda, CA  
 SEARCH-FLD: 435/69.1, 69.3, 240.2, 252.3, 320.1; 514/2; 536/22.1,  
 23.1, 23.2, 23.4, 23.7

## ABSTRACT:

The invention features a polypeptide consisting of amino acids 379-535 of diphtheria toxin, and portions thereof. This region, shown by X-ray crystallographic analysis to comprise the receptor binding domain of diphtheria toxin, is used as an immunogen and clinical therapeutic against diphtheria.

US PAT NO: 5,843,444 [IMAGE AVAILABLE] L14: 12 of 37  
 TITLE: Conjugate vaccine for group B streptococcus  
 DATE ISSUED: Dec. 1, 1998  
 INVENTOR: James L. Michel, Waban, MA  
 Dennis L. Kasper, Newton, MA  
 Frederick M. Ausubel, Newton, MA  
 Lawrence C. Madoff, Boston, MA  
 SEARCH-FLD: 424/165.1, 197.11, 244.1; 435/69.3; 530/403; 536/23.7,  
 123.1

## ABSTRACT:

A vaccine capable of protecting a recipient from infection caused by group B Streptococcus. The vaccine provides polysaccharide-protein moieties and contain (a) a group B Streptococcus polysaccharide conjugated to (b) a functional derivative of a group B Streptococcus C protein alpha antigen that retains the ability to elicit protective antibodies against group B Streptococcus. The vaccine may contain only one type of such polysaccharide-protein unit or may contain a mixture of more than one type of unit.

US PAT NO: 5,830,710 [IMAGE AVAILABLE] L14: 13 of 37  
 TITLE: Cloned porphyromonas gingivalis genes and probes for the  
 detection of periodontal disease  
 DATE ISSUED: Nov. 3, 1998  
 INVENTOR: Ann Progulske-Fox, Gainesville, FL  
 Somying Tumwasorn, Bangkok, Thailand  
 Guylaine Lepine, Fort Erie, Canada

Searcher : Shears 308-4994

09/120044

Naiming Han, Gainesville, FL  
Marilyn Lantz, Indianapolis, IN  
Joseph M. Patti, Missouri City, TX  
SEARCH-FLD: 424/190.1, 234.1; 435/91.1; 536/22, 22.1, 23.2

ABSTRACT:

DNA fragments from Porphyromonas gingivalis which express proteins that elicit anti-P. gingivalis immunologic responses are described. Microorganisms, genetically modified to express P. gingivalis antigens, are provided. Also disclosed are probes, vaccines, and monoclonal antibodies for the detection and prevention of periodontal disease.

US PAT NO: 5,824,791 [IMAGE AVAILABLE] L14: 14 of 37  
TITLE: Cloned porphyromonas gingivalis genes and probes for the detection of periodontal disease

DATE ISSUED: Oct. 20, 1998  
INVENTOR: Ann Progulske-Fox, Gainesville, FL  
Somying Tumwasorn, Bangkok, Thailand  
Guylaine Lepine, Fort Erie, Canada  
Naiming Han, Gainesville, FL  
Marilyn Lantz, Indianapolis, IN  
Joseph M. Patti, Missouri City, TX  
SEARCH-FLD: 536/22.1, 23.7; 435/256.1, 252.3

ABSTRACT:

DNA fragments from Porphyromonas gingivalis which express proteins that elicit anti-P. gingivalis immunologic responses are described. Microorganisms, genetically modified to express P. gingivalis antigens, are provided. Also disclosed are probes, vaccines, and monoclonal antibodies for the detection and prevention of periodontal disease.

US PAT NO: 5,820,860 [IMAGE AVAILABLE] L14: 15 of 37  
TITLE: Conjugate vaccine for group B streptococcus  
DATE ISSUED: Oct. 13, 1998  
INVENTOR: James L. Michel, Waban, MA  
Dennis L. Kasper, Newton Centre, MA  
Frederick M. Ausubel, Newton, MA  
Lawrence C. Madoff, Boston, MA

SEARCH-FLD: 424/165.1, 197.11; 435/69.3, 172.1; 530/350, 403, 825;  
536/23.7

ABSTRACT:

A vaccine capable of protecting a recipient from infection caused by group B Streptococcus. The vaccine provides polysaccharide-protein moieties and contain (a) a group B Streptococcus polysaccharide conjugated to (b) a functional derivative of a group B Streptococcus C protein alpha antigen that retains the ability to elicit protective antibodies against group B Streptococcus. The vaccine may contain only one type of such polysaccharide-protein unit or may contain a mixture of more than one type of unit.

US PAT NO: 5,804,193 [IMAGE AVAILABLE] L14: 16 of 37  
Searcher : Shears 308-4994

09/120044

TITLE: Truncated PSPA lacking a functional cell membrane anchor region  
DATE ISSUED: Sep. 8, 1998  
INVENTOR: David E. Briles, Birmingham, AL  
Janet L. Yother, Birmingham, AL  
SEARCH-FLD: 424/190.1, 244.1, 197.11, 200.1; 530/350, 825; 435/252.3

ABSTRACT:

A purified pneumococcal surface protein A (PspA) comprises a truncated form of the PspA protein which is immunoprotective and contains the protective epitopes of PspA. The PspA protein is soluble in physiologic solution and lacks at least the cell membrane anchor region of the whole protein. The protein is formed by insertion-duplication of mutagenesis of *S. pneumoniae* with *pspA* gene and expression of the truncated protein into the growth medium.

US PAT NO: 5,800,821 [IMAGE AVAILABLE] L14: 17 of 37  
TITLE: Bacterial spores as a heat stable vaccine delivery system  
DATE ISSUED: Sep. 1, 1998  
INVENTOR: David W. K. Acheson, Norwood, MA  
Abraham L. Sonenshein, Brookline, MA  
Gerald T. Keusch, Lexington, MA  
SEARCH-FLD: 424/246.1, 200.1, 247.1, 234.1, 93.46, 93.41

ABSTRACT:

A method of stimulating a vertebrate animal to produce an immune response to at least one antigen is described. The method includes genetically engineering a bacterial cell with DNA encoding at least one antigen and inducing the bacterial cell to sporulate, then orally administering the bacterial spores to an animal. The bacterial spores germinate in the gastrointestinal tract of the animal and express the antigen so that it comes into contact with the animal's immune system and elicits an immune response.

US PAT NO: 5,783,386 [IMAGE AVAILABLE] L14: 18 of 37  
TITLE: Mycobacteria virulence factors and a novel method for their identification  
DATE ISSUED: Jul. 21, 1998  
INVENTOR: William R. Jacobs, Jr., City Island, NY  
Barry R. Bloom, Hastings-on-Hudson, NY  
Desmond Michael Collins, Wellington, New Zealand  
Geoffrey W. de Lisle, Wellington, New Zealand  
Lisa Pascopella, Hamilton, MT  
Riku Pamela Kawakami, Wellington, New Zealand  
SEARCH-FLD: 435/6, 91.2, 172.1; 424/248.1

ABSTRACT:

Polynucleotides associated with virulence in mycobacteria, and particularly a fragment of DNA isolated from *M. bovis* that contains a region encoding a putative sigma factor. Also provided are methods for a DNA sequence or sequences associated with virulence determinants in

Searcher : Shears 308-4994

mycobacteria, and particularly in *M. tuberculosis* and *M. bovis*. The invention also provides corresponding polynucleotides associated with avirulence in mycobacteria. In addition, the invention provides a method for producing strains with altered virulence or other properties which can themselves be used to identify and manipulate individual genes.

US PAT NO: 5,753,463 [IMAGE AVAILABLE] L14: 19 of 37  
 TITLE: Structural gene of pneumococcal protein  
 DATE ISSUED: May 19, 1998  
 INVENTOR: David E. Briles, Birmingham, AL  
 Janet L. Yother, Birmingham, AL  
 SEARCH-FLD: 435/69.3, 252.33, 252.3, 253.4, 320.1, 844, 885, 253.1;  
 536/23.7; 530/416, 417

## ABSTRACT:

A purified pneumococcal surface protein A (PspA) comprises a truncated form of the PspA protein which is immunoprotective and contains the protective epitopes of PspA. The PspA protein is soluble in physiologic solution and lacks at least the cell membrane anchor region of the whole protein. The protein is formed by insertion-duplication of mutagenesis of *S. pneumoniae* with *pspA* gene and expression of the truncated protein into the growth medium.

US PAT NO: 5,714,374 [IMAGE AVAILABLE] L14: 20 of 37  
 TITLE: Chimeric rhinoviruses  
 DATE ISSUED: Feb. 3, 1998  
 INVENTOR: Edward V. Arnold, New Brunswick, NJ  
 Gail Ferstandig Arnold, New Brunswick, NJ  
 SEARCH-FLD: 435/235.1, 172.3; 424/93.2, 93.6, 199.1

## ABSTRACT:

Various novel recombinant chimeric human rhinoviruses are disclosed, including viruses comprising human rhinovirus 14 into which chimeric regions derived from influenza HA, poliovirus and HIV-1 have been incorporated. Chimeric human rhinoviruses are particularly advantageous as they are only mildly pathogenic, have numerous potential serotypes and can elicit significant mucosal and serum immunological response. Design considerations, methods, and examples are described. The chimeric rhinoviruses can be used as vaccines and for a variety of other immunotechnological applications including passive immunization, immunodiagnostic testing and antigenicity and immunogenicity studies.

US PAT NO: 5,693,622 [IMAGE AVAILABLE] L14: 21 of 37  
 TITLE: Expression of exogenous polynucleotide sequences cardiac muscle of a mammal  
 DATE ISSUED: Dec. 2, 1997  
 INVENTOR: Jon A. Wolff, Madison, WI  
 David J. Duke, Salem, OR  
 Philip L. Felgner, Rancho Santa Fe, CA  
 SEARCH-FLD: 514/44; 935/53, 55, 56, 60

## ABSTRACT:

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09/120044

The present invention provides a method for delivering a pharmaceutical polypeptide to the interior of a cardiac cell of a vertebrate in vivo, comprising the step of introducing a preparation comprising a pharmaceutically acceptable injectable carrier and naked polynucleotide operatively coding for the polypeptide into the interstitial space of the heart, whereby the naked polynucleotide is taken up into the interior of the cell and has a pharmacological effect on the vertebrate. In a preferred embodiment wherein the polynucleotide encodes polypeptide immunologically foreign to the vertebrate, the delivery method preferably comprises delivering an immunosuppressive agent to the vertebrate to limit immune responses directed to the polypeptide.

US PAT NO: 5,679,515 [IMAGE AVAILABLE] L14: 22 of 37  
TITLE: Mycobacterial reporter strains and uses thereof  
DATE ISSUED: Oct. 21, 1997  
INVENTOR: Charles Kendall Stover, Mercer Island, WA  
Mark Jeffrey Hickey, Seattle, WA  
SEARCH-FLD: 435/8, 253.1, 320.1, 6, 32, 252.3

ABSTRACT:

This invention relates to a method of quantifying bacteria in vivo or in vitro using bacterial reporter strains. In particular this invention provides a method utilizing mycobacterial reporter strains that permits rapid screening for in vivo antimycobacterial activity of various compositions. In addition this invention provides for particular mycobacterial reporter strains expressing the FFlux gene at levels sufficiently high to allow detection in tissue homogenates without lysis or concentration of the bacteria.

US PAT NO: 5,663,317 [IMAGE AVAILABLE] L14: 23 of 37  
TITLE: Microorganism having attenuated invasiveness  
DATE ISSUED: Sep. 2, 1997  
INVENTOR: Stanley Falkow, Portola Valley, CA  
Catherine A. Lee, Newton, MA  
SEARCH-FLD: 536/23.7; 435/252.3, 252.8, 172.3, 320.1; 935/9, 11, 65

ABSTRACT:

The invention provides nucleic acids encoding one or more hyper-invasive genes within the hil locus (hyper-invasion locus) or fragments thereof, methods for making attenuated microorganisms and identifying such hyper-invasive nucleic acids as well as mutant microorganisms wherein one or more hyper-invasive genes within the hil locus are modified to attenuate the invasive phenotype of the microorganism. The methods of the invention utilize conditions which repress invasiveness in an otherwise invasive microorganism. The method comprises mutating an invasive microorganism to form a plurality of mutant microorganisms. The thus formed mutants are exposed to conditions which repress invasiveness of the parental invasive microorganism. At least one mutant microorganism is then detected which exhibits an increase in invasiveness as compared to the parental invasive microorganism. The site of mutation in the genome

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of the mutant microorganism is then determined to localize and identify one or more hyper-invasive genes within the hil locus of the invasive microorganism.

US PAT NO: 5,662,908 [IMAGE AVAILABLE] L14: 24 of 37  
 TITLE: Invasive microorganisms  
 DATE ISSUED: Sep. 2, 1997  
 INVENTOR: Stanley Falkow, Portola Valley, CA  
 Ralph Isberg, Brookline, MA  
 Virginia Miller, Van Nuys, CA  
 Joseph W. St. Geme, III, Redwood City, CA  
 Catherine A. Lee, Newton, MA  
 SEARCH-FLD: 435/172.1, 172.3, 252.3, 252.8, 879; 424/92, 93A, 200.1,  
 235.1, 258.1

#### ABSTRACT:

Novel methods and microorganisms are provided, where novel genetic mammalian cell invasive capability is imparted to a microorganism by the introduction of an exogenous ail or hil gene. The resulting organisms are then capable of binding to mammalian cells and are transferred to the cytoplasm. Other novel genetic capabilities may be imparted to the unicellular microorganism, which may serve as a vaccine for one or more pathogens or may introduce genetic capabilities or foreign molecules into a mammalian host cell. The sequences may be used for an in vitro screen for pathogenicity. Mutant microorganisms having an attenuated invasive phenotype are also disclosed wherein one or more invasive genes have been modified.

US PAT NO: 5,648,241 [IMAGE AVAILABLE] L14: 25 of 37  
 TITLE: Conjugate vaccine against group B streptococcus  
 DATE ISSUED: Jul. 15, 1997  
 INVENTOR: James L. Michel, Waban, MA  
 Dennis L. Kasper, Newton Centre, MA  
 Frederick M. Ausubel, Newton, MA  
 Lawrence C. Madoff, Boston, MA  
 SEARCH-FLD: 536/23.7; 435/252.33, 253.4, 172.3, 69.3, 320.1

#### ABSTRACT:

A purified DNA molecule is disclosed that comprises a DNA sequence encoding a Group B Streptococcus alpha antigen or antibody eliciting fragment. The alpha antigen sequence encodes several distinct domains including an N-terminal sequence that precedes the start of the alpha antigen repeating sequence, a C-terminal anchor sequence and a repeating unit motif. The ability to protect mice against a Streptococcus infection with antisera against cellular extracts containing the alpha antigen encoded by the DNA molecule was determined.

US PAT NO: 5,554,372 [IMAGE AVAILABLE] L14: 26 of 37  
 TITLE: Methods and vaccines comprising surface-active copolymers  
 DATE ISSUED: Sep. 10, 1996  
 INVENTOR: Robert L. Hunter, Tucker, GA  
 SEARCH-FLD: 424/280.1, 283.1, 278.1, 279.1, 78.38; 514/723, 772.3  
 Searcher : Shears 308-4994

## ABSTRACT:

The present invention comprises adjuvants which, when admixed with an antigen and administered into a human or animal, will induce a more intense immune response to the antigen than when the antigen is administered alone. In many cases, the adjuvant that is described as the present invention will increase overall titer of antibodies of a specific isotype which are specific for the antigen. For example, in mice, when the adjuvant of the present invention is admixed with a conventional antigen, the isotype that is induced in the mouse is changed from a predominantly IgG1 isotype to the more protective IgG2 isotype and, in some cases, IgG3 isotype. Thus, by practicing the present invention, one can improve the overall protective effect of conventional vaccines.

US PAT NO: 5,541,100 [IMAGE AVAILABLE] L14: 27 of 37  
 TITLE: Chimeric rhinoviruses  
 DATE ISSUED: Jul. 30, 1996  
 INVENTOR: Edward V. Arnold, New Brunswick, NJ  
 Gail F. Arnold, New Brunswick, NJ  
 SEARCH-FLD: 435/235.1, 172.3; 424/93.6

## ABSTRACT:

Recombinant chimeric human rhinovirus and method for stimulation of a specific immune response. Design considerations, methods, and examples are described. Chimeric rhinoviruses can be used as vaccines and for a variety of other immunotechnological applications.

US PAT NO: 5,476,929 [IMAGE AVAILABLE] L14: 28 of 37  
 TITLE: Structural gene of pneumococcal protein  
 DATE ISSUED: Dec. 19, 1995  
 INVENTOR: David E. Briles, Birmingham, AL  
 Janet L. Yother, Birmingham, AL  
 Larry S. McDaniel, Birmingham, AL  
 SEARCH-FLD: 536/23.7, 24.32, 24.33

## ABSTRACT:

A purified pneumococcal surface protein A (PspA) comprises a truncated form of the PspA protein which is immunoprotective and contains the protective epitopes of PspA. The PspA protein is soluble in physiologic solution and lacks at least the cell membrane anchor region of the whole protein. The protein is formed by insertion-duplication of mutagenesis of *S. pneumoniae* with *pspA* gene and expression of the truncated protein into the growth medium.

US PAT NO: 5,426,181 [IMAGE AVAILABLE] L14: 29 of 37  
 TITLE: DNA encoding cytokine-induced protein, TSG-14  
 DATE ISSUED: Jun. 20, 1995  
 INVENTOR: Tae H. Lee, Cambridge, MA  
 Gene W. Lee, New York, NY  
 Jan Vilcek, New York, NY  
 SEARCH-FLD: 435/69.1, 69.5, 240.1, 252.3, 243; 536/23.1, 23.5

09/120044

ABSTRACT:

Pleiotropic pro-inflammatory cytokines, such as TNF and IL-1, induce expression of a polypeptide molecule, termed TSG-14, in connective tissue cells. The TSG-14 polypeptide and functional derivatives thereof, DNA coding therefor, expression vehicles, such as a plasmids, and host cells transformed or transfected with the DNA molecule, and methods for producing the polypeptide and the DNA are provided. Antibodies specific for the TSG-14 polypeptide are disclosed, as is a method for detecting the presence of TSG-14 polypeptide in a biological sample, using the antibody or another molecule capable of binding to TSG-14 such as hyaluronic acid. A method for detecting the presence of nucleic acid encoding a normal or mutant TSG-14 polypeptide, a method for measuring induction of expression of TSG-14 in a cell using either nucleic acid hybridization or immunoassay, a method for identifying a compound capable of inducing the expression of TSG-14 in a cell, and a method for measuring the ability of a cell to respond to TNF are also provided.

US PAT NO: 5,338,842 [IMAGE AVAILABLE] L14: 30 of 37

TITLE: Yersinia INV nucleic acids

DATE ISSUED: Aug. 16, 1994

INVENTOR: Ralph R. Isberg, Brookline, MA  
Virginia Miller, Los Angeles, CA  
Stanley Falkow, Portola Valley, CA

SEARCH-FLD: 536/27, 23.7, 24.32; 435/172.3, 320.1, 252.3, 252.33, 6, 69.1; 935/11, 72, 173

ABSTRACT:

Novel methods and microorganisms are provided, where novel genetic mammalian cell invasive capability is imparted to a microorganism by the introduction of an exogenous inv gene. The resulting organisms are then capable of binding to mammalian cells and are transferred to the cytoplasm. Other novel genetic capabilities may be imparted to the unicellular microorganism, which may serve as a vaccine for one or more pathogens or may introduce genetic capabilities or foreign molecules into a mammalian host cell. The sequences may be used for an in vitro screen for pathogenicity.

US PAT NO: 5,310,654 [IMAGE AVAILABLE] L14: 31 of 37

TITLE: Method for determining virulence of Yersinia

DATE ISSUED: May 10, 1994

INVENTOR: Ralph R. Isberg, Brookline, MA  
Virginia Miller, Los Angeles, CA  
Stanley Falkow, Portola Valley, CA

SEARCH-FLD: 435/6, 252.33, 252.3, 320; 935/77, 78; 424/93; 536/23.7

ABSTRACT:

Novel methods and microorganisms are provided, where novel genetic mammalian cell invasive capability is imparted to a microorganism by the introduction of an exogenous inv or ail gene. The resulting organisms are then capable of binding to mammalian cells and are transferred to the cytoplasm. Other novel genetic capabilities may be imparted to the

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unicellular microorganism, which may serve as a vaccine for one or more pathogens or may introduce genetic capabilities or foreign molecules into a mammalian host cell. The sequences may be used for an in vitro screen for pathogenicity.

US PAT NO: 5,292,653 [IMAGE AVAILABLE] L14: 32 of 37  
 TITLE: Equine herpesvirus 1 tk mutants  
 DATE ISSUED: Mar. 8, 1994  
 INVENTOR: Malon Kit, Houston, TX  
 Saul Kit, Houston, TX  
 SEARCH-FLD: 435/320.1, 69.1; 935/32, 22

ABSTRACT:

The present invention relates to Equine Herpesvirus Type 1 mutants which fail to produce any functional thymidine kinase as a result of a deletion and/or insertion in the EHV-1 thymidine kinase gene.

US PAT NO: 5,275,814 [IMAGE AVAILABLE] L14: 33 of 37  
 TITLE: Allergen-thymic hormone conjugates for treatment of IgE mediated allergies  
 DATE ISSUED: Jan. 4, 1994  
 INVENTOR: Aristo Wojdani, Los Angeles, CA  
 SEARCH-FLD: 530/402, 403, 404, 405, 406, 408, 409, 410, 395, 397, 301, 399, 365, 370, 379; 424/88, 91, 92, 89, 93A, 93D; 435/174, 177; 574/2, 12, 8, 21, 54

ABSTRACT:

A protein conjugate or mixture useful in immunotherapy composed of a biological response modifier (BRM) and an allergen is disclosed. In use the protein conjugate or mixture is combined with a pharmaceutically acceptable carrier. Cytokines, bacterial, fungal and viral immunopotentiators and thymus hormones are disclosed as suitable BRM's for use in the invention.

US PAT NO: 5,239,066 [IMAGE AVAILABLE] L14: 34 of 37  
 TITLE: Yersinia ail nucleic acids  
 DATE ISSUED: Aug. 24, 1993  
 INVENTOR: St. Geme, III: Joseph W., Redwood City, CA  
 Stanley Falkow, Portola Valley, CA  
 Ralph Isberg, Brookline, MA  
 Virginia Miller, Van Nuys, CA  
 SEARCH-FLD: 536/27, 23.1, 23.7, 24.32; 435/172.3, 320.1, 69.1, 69.3, 6, 252.3; 935/9, 11

ABSTRACT:

Nucleic acids encoding all or part of a Yersinia ail gene are provided. The nucleic acid comprises at least 50 base pairs of a Yersinia ail gene in isolated form or consists of a fragment consisting essentially of at least 50 base pairs but not more than 50 kilo base pairs of a Yersinia ail gene. Such nucleic acids can also be operably linked to transcriptional and translational initiation and termination sequences which are functional in a microorganism host.

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US PAT NO: 5,116,612 [IMAGE AVAILABLE] L14: 35 of 37  
 TITLE: Immunotherapy agents for treatment of IgE mediated allergies  
 DATE ISSUED: May 26, 1992  
 INVENTOR: Aristo Wojdani, Los Angeles, CA  
 SEARCH-FLD: 424/88, 91, 92, 85.1, 85.2, 89, 85.4; 530/403, 404, 405, 406, 351, 409, 410

## ABSTRACT:

A protein conjugate or mixture useful in immunotherapy composed of a biological response modifier (BRM) and an allergen is disclosed. In use the protein conjugate or mixture is combined with a pharmaceutically acceptable carrier. Cytokines, bacterial, fungal and viral immunopotentiators and thymus hormones are disclosed as suitable BRM's for use in the invention.

US PAT NO: 4,946,945 [IMAGE AVAILABLE] L14: 36 of 37  
 TITLE: Immunotherapy agents for treatment of IgE mediated allergies  
 DATE ISSUED: Aug. 7, 1990  
 INVENTOR: Aristo Wojdani, Los Angeles, CA  
 SEARCH-FLD: 530/402, 403, 404, 405, 408, 409, 410, 390, 391; 424/85.91, 92, 88, 91, 93, 95; 514/2, 8, 12, 24

## ABSTRACT:

A protein conjugate or mixture useful in immunotherapy composed of a biological response modifier (BRM) and an allergen is disclosed. In use the protein conjugate or mixture is combined with a pharmaceutically acceptable carrier. Cytokines, bacterial, fungal and viral immunopotentiators and thymus hormones are disclosed as suitable BRM's for use in the invention.

US PAT NO: 4,808,700 [IMAGE AVAILABLE] L14: 37 of 37  
 TITLE: Immunogenic conjugates of non-toxic E. coli LT-B enterotoxin subunit and capsular polymers  
 DATE ISSUED: Feb. 28, 1989  
 INVENTOR: Porter W. Anderson, Rochester, NY  
 John D. Clements, New Orleans, LA  
 SEARCH-FLD: 530/403, 807, 812; 424/92; 935/12; 514/12

## ABSTRACT:

A conjugate, which is the reductive amination product of an immunogenic capsular polymer fragment, having a reducing end and derived from the capsular polymer of a bacterial pathogen, and the non-toxic polypeptide binding subunit of the heat-labile enterotoxin of Escherichia coli (LT-BNT). Also disclosed, are methods for the preparation of the conjugates and for the preparation of vaccines containing the conjugates which elicits an effective level of antibodies in humans. By administering an immunogenic amount of the conjugates, active immunization against systematic infection in young mammals caused by bacterial pathogens can be induced.

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              OR 56) OR PNV(W) (103 OR 207 OR 111 OR 211)

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